ELSEVIER

Do Elderly Patients Deserve a Kidney Graft?

P. Nunes, A. Mota, B. Parada, A. Figueiredo, F. Rolo, C. Bastos, and F. Macário

ABSTRACT

Purpose. Compare renal transplant long-term outcomes among recipients aged 60 years or older with those in younger patients.

Patients and methods. We analyzed 103 transplants in recipients above 60 years of age for the influence of key factors related to the graft and patient. The results were compared with 1060 transplant recipients aged 18 to 59 years.

Results. The mean ages were 62.93 and 40.35 years for the older and younger group. The older group showed a higher prevalence of obesity and unknown etiologies for the end-stage renal disease. Important comorbidity was significantly more frequent among recipients aged more than 60 years, mainly of a cardiovascular nature (56% vs 18.5%). Donor age (39.75 vs 31.59 years), cold ischemia time (22.43 vs 20.49 hours) and human leukocyte antigen compatibilities (2.59 vs 2.36) were significantly greater in the older subset. After a mean follow-up of 4.72 and 6.07 years for the older versus younger group, we found no differences in initial graft function, acute rejection rate, and serum creatinine/clearance. Patient and graft survivals at 1, 5, and 10 years were lower among the 60+ group. There were no differences in graft survival censored for death with a functioning graft, namely, 95.1%, 89.4%, and 81.2% for the 60+ cohort. The main cause of graft loss in the older group was death with a functioning graft.

Conclusion. Renal transplantation should be considered for selected patients older than 60 years. Despite a shorter life expectancy, they benefit from it similar to younger recipients.

THE INCIDENCE OF end-stage renal disease (ESRD) increases with advancing age. Patients older than 60 years represent between 53% and 66% of the population requiring renal replacement therapies.[1] Therapy for ESRD in the elderly is characterized by tremendous challenges, raising medical, ethical, and socioeconomic concerns. Hemodialysis, the most frequently used renal replacement modality in these patients, is associated with significant morbidity, mortality, and a poor quality of life.[2,3] The great organ shortage, higher comorbidity rate, and shorter life expectancy make the allocation of kidneys to this population controversial.

Nevertheless, transplantation is the gold standard treatment for ESRD patients. With immunosuppression based upon calcineurin inhibitors, it has become a feasible alternative for the elderly population.[4–7] Compared with hemodialysis, renal transplantation is associated with a 61% decrease in the long-term risk of death and an additional 4-year life expectancy for patients over 60 years.[4]

In this retrospective study, we report a single-center, long-term follow-up of kidney transplants in patients above

From the Department of Urology and Renal Transplantation, Hospitais da Universidade de Coimbra, Coimbra, Portugal.

Address reprint requests to Pedro Nunes, Department of Urology and Renal Transplantation, Hospitais da Universidade de Coimbra, 3000 Coimbra, Portugal. E-mail: pedro.nunes@sapo.pt

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60 years of age. The main objectives of this study were to analyze whether long-term patient and graft survival rates supported a policy of cadaveric kidney transplantation for these patients in our center, and to identify potential differences from a population of younger recipients.

PATIENTS AND METHODS

Between June 1980 and December 2003, 1227 kidney transplantations were performed in 1190 patients, including 1060 (86.4%) transplants in patients aged 18 to 59 years, and 103 (8.4%), 60 years or older. Recipients younger than 18 years were excluded from the study.

Routine pretransplant cardiocirculatory evaluation of recipients older than 60 years included cardiac ultrasound, stress thallium test, and coronary angiography. Peripheral Doppler studies were performed when indicated. Creatinine clearance was calculated using the Cockroft and Gault formula.

For each group we explored the main factors related to the recipients, donors, and procedures. Actuarial survivals of patients and grafts were calculated at 1, 5, and 10 years for comparison between the two groups.

Statistical analysis was performed using SPSS for Windows 10.0. Categorical parameters were compared by χ^2 testing, and continuous variables, by Student *t* test with Yates's correction or by Fisher exact test wherever appropriate. Cumulative actuarial survival and survival curves for grafts and patients were calculated by Kaplan-Meier analysis and tested for differences with the Mantel-Cox log-rank test. A *P* value of $<.05$ was considered significant. The most important demographic and transplantation related data are displayed in Table 1.

We performed approximately 10 times more transplant procedures (1060 vs 103) in patients in the 18 to 59 group than in the 60+ years group. Mean age in the younger group was 40.35 years (SD 11.25) and in the older group 62.93 (SD 12.43). A predominance of male recipients was found in both subsets, with a slight preponderance in the older group. Average length of pretransplant renal replacement therapy was significantly longer in the 60+ group. Recipient weight was higher in the group aged more than 60 years leading to more prevalent obesity.

Unknown etiologies for the ESRD were more common in the 60+ group, and glomerular causes more frequent in the 18 to 59 group. The absence of important comorbidity was significantly more common in the 18 to 59 group. The main difference in the type of comorbidity was the rate of cardiovascular disease with 18.5% in the younger group versus 56% in the older one ($P < .001$). Donor age was significantly lower in the 18 to 59 group, namely 31.59 versus 39.75 years for the 60+ cohort. Human leukocyte antigen (HLA; A, B, DR) compatibility was greater in the older group. Mean cold ischemia time was higher for the kidneys in the 60+ group. Percentages of particular initial immunosuppressive schemes did not differ between both groups, reflecting overall department preferences at the time.

RESULTS

Most important results are depicted in Table 2. The mean follow-up was 4.72 for the older and 6.07 years for the younger recipients ($P < .05$). Initial graft function did not diverge between the two groups; with the great majority (76.6% to 80.6%) showing primary function. The rate of acute rejections was similar in both groups; approximately two-thirds of patients never had an episode. Although the mean number of acute rejections was slightly lower among

Table 1. Demographic and Transplantation-Related Data in the Two Groups

	Group		
	18–59	60+	*P*
Transplants (*n*)	1060	103	
Recipient age (years; mean ± SD)	40.35 ± 11.25	62.93 ± 12.43	<.001
Gender (male/female ratio)	66.7/33.3	79.6/20.4	NS
Months of pretransplant dyalisis (mean ± SD)	63.57 ± 11.44	67.54 ± 10.75	<.001
Recipient weight (kg; mean ± SD)	63.57 ± 11.44	67.54 ± 10.75	<.001
Obesity (%)	15.8	25.9	<.05
Max PRA > 40% (mean ± SD)	7.64 ± 14.61	6.29 ± 9.14	NS
Cause of ESRD (%)			
Unknown or undetermined	34.4	46.6	<.05
Glomerular	21.7	7.8	<.05
Multisystem disease	16.7	16.5	NS
Diabetes mellitus	8.1	8.0	NS
Arterial hypertension	7.9	8.0	NS
Cystic and congenital	14.2	14.6	NS
Tubulointersticial	13.0	14.6	NS
Comorbidity (%)			
No comorbidity	48.9	17.0	<.001
Cardiovascular disease	18.5	56.0	<.001
Donor age (years; mean ± SD)	31.59 ± 14.28	39.75 ± 18.20	<.001
Donor >60 years (%)	4.9	19.4	<.001
Donor creatinine (mg/dL; mean ± SD)	1.13 ± 0.44	1.17 ± 0.44	NS
Donor artificial ventilation time (hours; mean ± SD)	55.71 ± 54.45	50.42 ± 47.22	NS
HLA (A, B, DR) matches (1–6) (mean ± SD)	2.36 ± 1.00	2.59 ± 1.04	<.05
Cold ischemia time (hours; mean ± SD)	20.49 ± 6.56	22.43 ± 6.56	<.05

SD, standard deviation; NS, nonsignificant; PRA, panel-reactive antibodies; ESRD, end-stage renal disease; HLA, human leukocyte antigen.

the older group (0.33 vs 0.43), it did not reach statistical significance.

Graft function, as assessed by measuring the serum creatinine, was not significantly different between the two groups at 1 month and 1 and 5 years however, it was lower at 10 years in the older group (1.13 vs 1.52; $P < .05$). Creatinine clearance was always lower in the older group albeit not a significant difference. Actuarial cumulative patient survival at 1, 5, and 10 years was 96.1%, 89.5%, and 79.5% for patients 18 to 59 years and 88.8%, 72.8%, and 50.6% for patients 60+ ($P < .001$; Figure 1 A). Actuarial cumulative graft survival at 1, 5 and 10 years was 91.7%, 80% and 62.1% for patients 18–59 years and 85.9%, 64.8% and 41.2% for patients 60+ ($P < .001$; Fig 1B).

When observations were censored for patient death with a functioning graft, actuarial graft survival at 1, 5, and 10 years was 92.9%, 87.1%, and 79.47% for patients 18 to 59 years and 95.1%, 89.4%, and 81.2% for 60+ recipients ($P = .717$; NS; Fig 1C).

Main causes of graft loss differed between the two groups. In the younger recipients the leading cause (37.7%) was chronic graft dysfunction versus 16.7% in the 60+ group ($P < .001$). In the older group the major cause was death with a functioning graft (71.4%) of the cases (vs 34.4% in the 18 to 59 group; $P < .001$).

When comparing patient and graft survivals (recipients 18 to 59 and 60+ considered together) we observed significant differences depending on the donors age (<60 or >60 years; Fig 2). Recipient cumulative survival at 1, 5, and 10 years was, respectively, 95.7%, 89.2%, and 78.3% for donors <60 years and 91.9%, 74.04%, and 54.71% for donors >60 years ($P = .0025$; Fig 2A).

Graft survivals at 1, 5, and 10 years were 95.45%, 78.99%, and 61.70%, respectively, for donors <60 years and 90.32%, 61.75%, and 37.69% for donors >60 years ($P = .0018$; Fig 2B). When considering recipients older than 60 years only, we observed a graft survival at 1, 5, and 10 years of 87.80%, 68.94%, and 42.97% for donors <60 years and 77.14%, 39.44%, and 39.44% for donors >60 years, respectively ($P = .05$; Fig 2C).

Patient cumulative survival for this group (recipients 60+) at 1, 5, and 10 years was, respectively, 91.3%, 74.72%, and 51.04% for donors <60 years and 77.14%, 69.02%, and 69.02% for donors >60 years ($P = .276$; NS; Fig 2D).

DISCUSSION

The increasing number of ESRD patients of more than 60 years of age raises important questions regarding the choice of the ideal renal replacement therapy for this population.

Table 2. Comparative Results Among the Two Groups of Recipients (18–59 Years Old and Older Than 60)

	Group		
	18–59	60+	*P*
Surgery duration (<3 h/>3 h; %)	67.2/32.8	67.7/32.3	NS
Follow-up (years; mean ± SD)	6.07 ± 4.58	4.72 ± 3.72	<.05
Initial graft function (%)			
Initial diuresis	80.6	76.6	NS
Acute tubular necrosis	16.6	21.4	NS
Never-functioning kidney	2.8	2.0	NS
Acute rejections (%)			
0	62.3	69.5	NS
1	33.1	28.0	NS
2	4.1	2.5	NS
3	0.5	0	NS
Acute rejections (mean ± SD)	0.43 ± 0.60	0.33 ± 0.52	NS
Recipient creatinine (mg/dL; mean ± SD)			
1 month	1.63 ± 1.15	1.80 ± 1.12	NS
1 year	1.38 ± 0.49	1.35 ± 0.45	NS
5 years	1.49 ± 0.70	1.32 ± 0.60	NS
10 years	1.52 ± 0.99	1.13 ± 0.15	<.05
Creatinine clearance (mL/min; mean ± SD)			
1 year	68.28 ± 19.63	64.70 ± 17.44	NS
5 years	71.3 ± 22.98	66.66 ± 19.27	NS
10 years	73.41 ± 22.46	64.63 ± 8.43	NS
Causes of graft loss (%)			
Graft chronic dysfunction	37.7	16.7	<.001
Death with a functioning graft	34.4	71.4	<.001
Causes of patient death			
Cardiovascular (%)	41.2	56.3	NS
Infection	25.7	34.4	NS
Neoplasic	12.2	3.1	NS

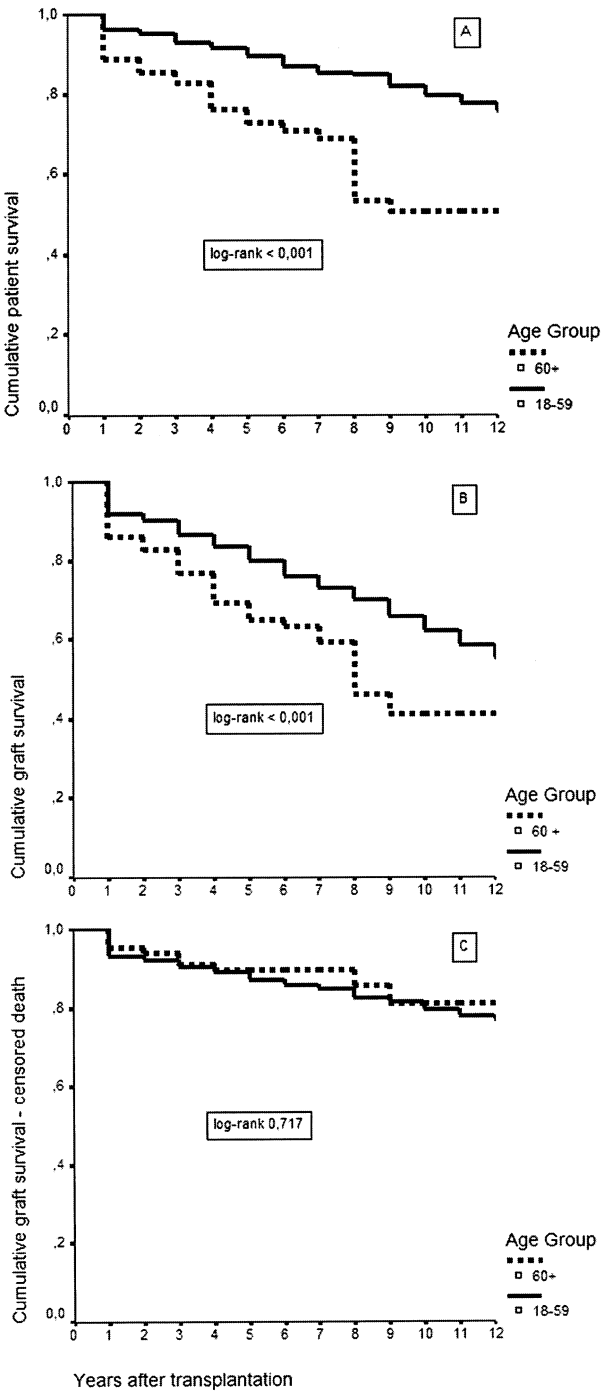

Fig. 1. Kaplan-Meier analysis and log-rank test comparison of patient survival **(A),** graft survival **(B),** and graft survival censored for patient death with functioning kidney **(C),** after renal transplantation according to the age group of recipient (18–59: continuous line; 60+: dashed line).

Comparisons between dialysis and transplantation are usually confused by a selection bias, leading the healthier patients to be grafted and the least fit ones to rest on dialytic therapies. In a period of organ shortage the great majority of units are still reluctant to accept elderly patients for renal transplantation because of their shorter life expectancy and higher comorbidity.

There are, however, several studies published where transplantation, even with marginal donors, has been shown to provide a clear advantage in terms of patient survival, quality of life, and cost-effectiveness, compared with maintenance hemodialysis.[8–10] Based on data from the literature we can state that short-term patient and graft survival is good in elderly renal failure patients,[3,5] despite the lower percentage of kidneys from living donors in the great majority of units. The few studies published with long-term results in this particular population[7,11,12] demonstrated patient and graft survivals at 5 years ranging, respectively, from 64% to 78% and 50% to 68%. Our results of 5-year patient survival of 72.8% and graft survival of 64.8% reflect one of the best survivals published.

Longer-term graft survival is decreased in the older transplant recipients; patient death with a functioning kidney is the major cause of graft loss. Performance of the graft seems to be excellent; we report a better graft survival censored for death with a functioning kidney for the population aged 60 or older when compared with the younger group, although without statistical relevance. Renal function was good in these grafts, based on the measured serum creatinine and calculated creatinine clearance, without differences compared to a younger population. The lower rate of acute rejection episodes in older recipients may explain this good performance of grafts.

Aging is described to be accompanied by a senescence of the immune system and a lower incidence of acute rejections.[11] There are, however, some reports where aged recipients had a rejection rate higher than younger controls, ranging from 40% to 70%.[13,14] This can be partially explained, in these studies, by worse compatibility in terms of HLA mismatches presented by the elderly subset of patients. The relationship connecting HLA matching and rate of acute rejections is well known[14] and can be one of the reasons for the few episodes experienced by our elderly recipients, who had a better compatibility compared to the younger ones.

Our older population was enriched for some factors that could predict a poorer outcome, like: higher obesity prevalence,[15,16] longer pretransplant dialysis period, higher mean donor age, longer cold ischemia time, and higher comorbidity prevalence mainly of cardiovascular nature. Some authors have reported these fact,[17] and described protocols to evaluate and correct cardiovascular risk factors,[5,11] seeking to minimize the main cause of death in this population.

No living donors were employed for patients of more than 60 years. The age group of donors (younger or older than 60 years) influenced the patient and graft survivals of the recipients when considered together. The importance of donor age has been described in several works[18] and the advantage of age-matching underlined.[19] Our elderly pa-

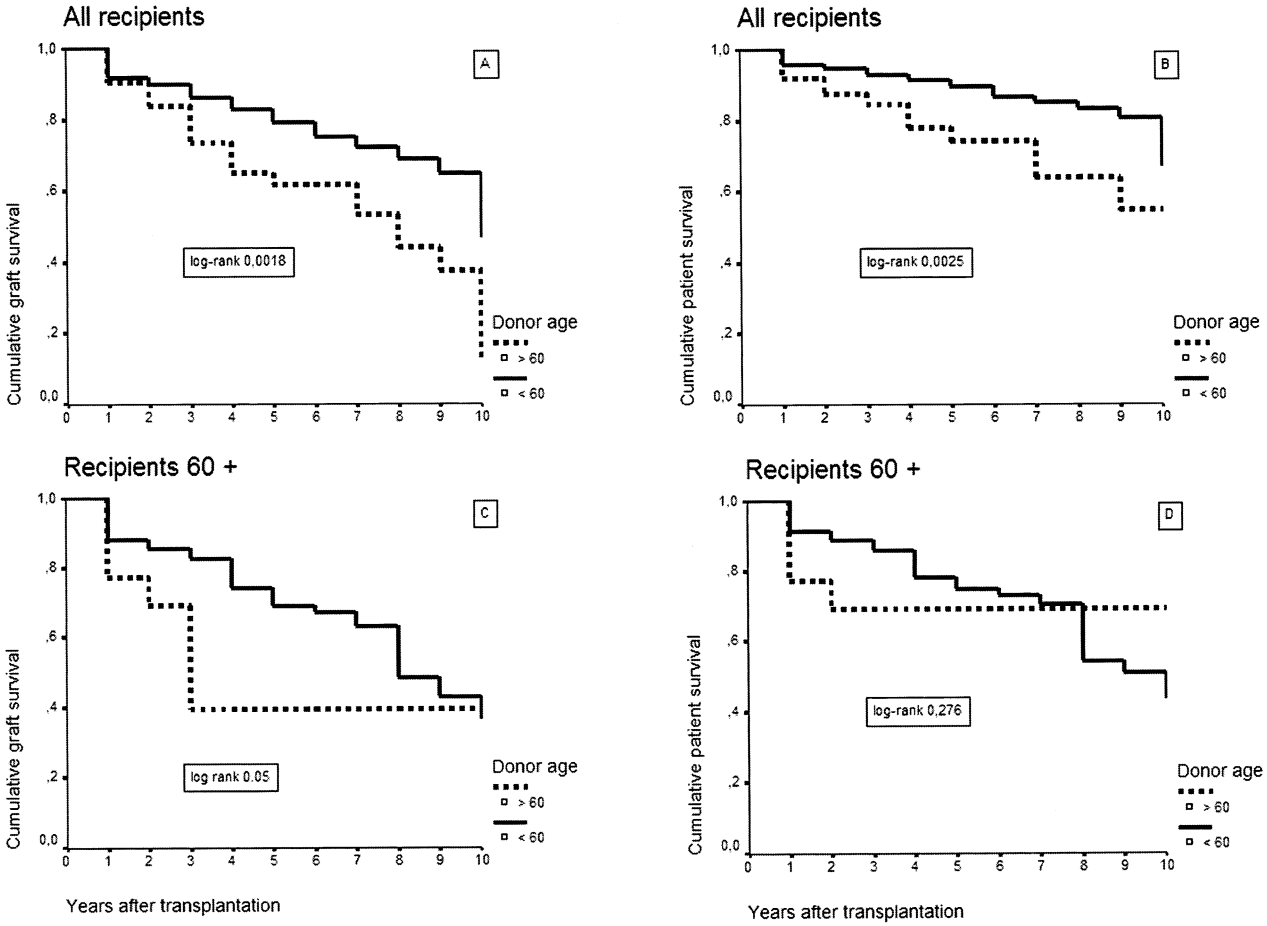

Fig. 2. Kaplan-Meier analysis and log-rank test comparison of graft and patient survival according to the age group of donors (<60: continuous line; >60: dashed line). Analysis of all the recipients older than 18 (**A** and **B**) and just the 60+ recipients (**C** and **D**).

tients, and as a result of our effort to age-match grafts and recipients, had a greater probability of receiving a kidney from a donor older than 60 years.

Donor age had little influence on graft survival in the older recipient group and no influence on patient survival. We conclude, like others,[11] that donor age is less important in elderly patients: the potentially short graft survival does not affect patient survival.

Contradicting this idea, Basar et al[20] clearly showed inferior outcomes when elderly donor grafts were used in older recipients, seeming that there is an added phenomenon of harmful factors. Based on our results, we recommend an old-for-old program,[13] where ABO-compatible organs from elderly donors with a negative cross-match, are locally allocated to old recipients.

In our experience, cadaveric kidney transplantation in selected patients over the age of 60 is a safe and effective method to treat ESRD. Age per se is not a contraindication for this kind of therapy. The effects of donor age are less prominent in this population and do not seem to influence patient survival.

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